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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,670	05/02/2001	Barry C. Finzel	6263.N	4815

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 12/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM. SM.

Office Action Summary	Application No.	Applicant(s)	
	09/847,670	FINZEL ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-43 and 47-59* is/are pending in the application.

4a) Of the above claim(s) *31-37,47 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-43 and 49-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *31-43 and 47-59* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendments and remarks, filed 10/16/03, are acknowledged. Amended claims 39, 41, and 49 and new claims 50-59 are acknowledged.

Applicant's arguments, filed 10/16/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

As stated in the previous two office actions, the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to crystals, crystallographic structure, and methods whereas in contrast the elected claims do not contain methods. Once product claims become allowable, the practice of rejoinder regarding method claims is acknowledged. At that time it would be appropriate to add "methods" into the title of the claimed invention.

The request for republishing, filed 10/16/03, has been forwarded for action to the PG Publishing section.

Claims 38-43 and 49-59 are herein under examination.

Claims Rejected Under 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF WRITTEN DESCRIPTION

Claims 55-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 55-57 recite the phrase "comprising atoms arranged in a spatial relationship represented by" which does not appear to have written support in the specification. The specification does mention "spatially distributed points" on page 19, line 22, and "'Structural equivalence,' as the term is used herein, describes a relationship between the three-dimensional structures of two molecules or portions thereof, e.g., two crystal structures" on page 21, lines 21-23 which encompasses relationships between structures and not individual atoms. However, the scope of the new claim limitations "comprising atoms arranged in a spatial relationship represented by" appears to differ from the scope of any support given in the specification. Thus, this phrase does not contain adequate written basis in the specification, original claims, or figures as originally filed and is considered NEW MATTER.

LACK OF ENABLEMENT

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

The rejection of claims 42, 43, and 49 is maintained and newly applied to new claims 50, 52, and 55-59 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

The rejection is maintained (for claims 42, 43, and 49), necessitated by amendment (for new claims 50, 51, 52, and 55-59), and reiterated below for reasons of record.

Although Applicants have disclosed information to enable one skilled in the art to make the tetragonal and orthorhombic crystals of crystalline Hepatitis C virus helicase with unit cell dimensions a = b = 109 Å ± 3 Å; c = 84 Å ± 2 Å; $\alpha = \beta = \gamma = 90°$; and space group $P4_1$ as well as a = 66 Å ± 2 Å; b = 110 Å ± 3 Å; c = 64 Å ± 2 Å; $\alpha = \beta = \gamma = 90°$; and space group $P2_12_12$,

respectively, the specification does not reasonably provide enablement for other crystalline Hepatitis C virus helicases and compositions comprising the same as stated in claims 42, 43, 49-52, and 55-59. The claims are broader than the enablement provided by the disclosure with regard to the large number of possible crystalline helicases that could be made. As the science of protein crystallization is well known to be a trial and error procedure with unpredictable results (Drenth, page 1, lines 13-20), one skilled in the art would require clear and precise guidance to make any particular crystal. Accordingly, it would be very difficult for a skilled artisan to make crystal structures of other crystalline Hepatitis C virus helicases or co-complexes beyond those mentioned in the instant case where specific coordinates are disclosed. Due to the unpredictability and difficulty of crystallizing proteins, it is unlikely that one of skill in the art would be able to make another crystal relying solely on the information for the two crystals disclosed in the specification without undue experimentation. Also, the information provided in Examples 4 and 5, pages 49-50, does not sufficiently enable a skilled artisan to make compositions comprising crystalline Hepatitis C virus helicase as no specific chemical entities or ligands were mentioned. Again, due to the unpredictability in the art, a skilled artisan could not reasonably expect to make such co-crystalline complexes based on generic guidelines without undue experimentation.

Applicants argue the MPEP states a specification that contains a teaching of the manner and process of making and using in terms which correspond in scope to those used in the describing and defining the subject matter sought to be patented must be taking in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein (MPEP § 2164.04). This is found

unpersuasive as the specification describes subject matter which is not enabled due to the unpredictability of crystallization. Due to the unpredictability and the difficulty in the art for crystallizing proteins, the specification only adequately describes how to make and use the specific crystalline structures mentioned with specific unit cell dimensions and space groups. Applicants argue that the MPEP 2164.01(b) states enablement under 35 USC 112, first paragraph, is satisfied if at least one method for making and using the claimed invention bears a reasonable correlation to the entire scope of the claim. This is found unpersuasive in the unpredictable and difficult art of crystallizing proteins. Applicants argue that for a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of the skill, state of the art and the information in the specification) would expect the genus could be used in that manner without undue experimentation and proof of enablement for other members of the claimed genus will be required where adequate reasons are advanced by the examiner that a person skilled in the art could not use the genus as a whole without undue experimentation as stated in MPEP 2164.02. This is found unpersuasive as the state of the art of making crystals is was not in a state of predictability at the time the invention was made and undue burden would be placed on a person skilled in the art to attempt to make crystals other then those specifically mentioned in the specification due to the trial and error procedure required (see Drenth, page 1, lines 13-20). Applicants also argue that the MPEP 2164.03 states even in unpredictable arts, a disclosure of every operable species is not required. This is found unpersuasive for various reasons. It is noted that MPEP 2164.03 also states the amount of guidance needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in

the art. The more that is known in the prior art about the nature of the invention, how to make and use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In the instant application, due to the unpredictability of the subject matter, only the specifically defined crystals which have been shown and described as having been crystallized satisfy the enablement rejection. MPEP 2164.03 also states the scope of the required enablement varies inversely with the degree of predictability involved. This section of the MPEP further states in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims.

Applicants argue that the Examiner has not provided any reason to doubt the objective truth of the disclosure provided in the specification. This is found unpersuasive as the specification provides reasonable enablement for the specific mentioned crystallized proteins by the fact that they were successfully synthesized and documented in the specification, but the trial and error procedure of this unpredictable art, supported by Drenth, causes a lack of enablement for the other crystalline structures encompassed in the claims.

LACK OF WRITTEN DESCRIPTION

The rejection of claims 38-43 and 49 is maintained and newly applied to claims 50-59 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

This rejection is reiterated below and maintained for reasons of record.

Claims 38-43 and 49-59 are directed to crystalline Hepatitis C virus helicases and compositions comprising the same. There is no disclosure regarding any crystals other than the tetragonal crystal having unit cell dimensions of a = b = 109 Å ± 3 Å; c = 84 Å ± 2 Å; $\alpha = \beta = \gamma$ = 90°; and space group $P4_1$ as well as the orthorhombic crystal having unit cell dimensions of a = 66 Å ± 2 Å; b = 110 Å ± 3 Å; c = 64 Å ± 2 Å; $\alpha = \beta = \gamma = 90°$; and space group $P2_12_12$. Claims 49 and 52 do not appear to be limited to any particular unit cell dimensions. Open claim language, such as "comprising" or "comprises" (claims 38, 40, 43, 50, 51, and 55-59 and dependent claims 39 and 41 therefrom) and "having" (claims 38, 42, 53, and 54, and dependent claims 39 and 43 therefrom), suggests the claims may contain other crystals which do not meet the written description provision of 35 USC 112, first paragraph. Applicants have not sufficiently described other crystals and compositions in such full, clear, and concise terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

The specification discloses SEQ ID NO: 1 which corresponds to an amino acid sequence of Hepatitis C virus helicase. SEQ ID NO: 1 meets the written description provisions of 35 USC 112, first paragraph. However, due to the facts that "having" (claim 42) and "comprising" (claims 43, 50, and 51) are open claim language which may contain the entire sequence plus additional unspecified sequence, these claims are directed to encompass amino acid sequences other than SEQ ID NO: 1 which do not meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 1 and the specifically mentioned crystals, but not the full breadth of the claims 38-43 and 49-59 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

This rejection is maintained for claims (38-43 and 49) and necessitated by amendment for the new claims (50-59).

Applicants agree that some of the instant claims use open claim language which means that the crystalline Hepatitis C virus helicase must include the subject matter described in the

claim, and may optionally include additional subject matter (i.e. other crystals). Applicants state the Examiner has not provided any convincing reasons or rationale as to why the subject matter does not meet the written description provision of 35 U.S.C. 112, first paragraph, but instead has focused on lack of written description for what is not recited in the claims. Applicants suggest the rejection is not a written description rejection but rather is based on the use of "comprising" and "having" as transitional phrases. Applicants further state these phrases are proper and acknowledged by the M.P.E.P. It is acknowledged that "comprising" and "having" are transitional phrases sometimes used in claim language of patent applications. However, in the instant application the use of these phrases creates claims that are broader and encompass more subject matter than the support that is provided by the written description. These phrases were pointed out to applicants so that they were made aware of where the lack of written description occurs in this application. Applicants were told what crystals and sequence they have support for in the application, what the claims encompass, and why the entire scope encompassed by the claims is not adequately supported by the written description.

Applicants argue that the claims regarding the amino acid sequence can only include the entire protein sequence. This is found unpersuasive as the claim language "*the* amino acid sequence" can be reasonably interpreted to include fragments of the sequence. Applicants are encouraged to amend the claim language to clarify that the entire sequence is what is, in fact, being claimed within the instant invention.

Applicants state the Examiner's use of the phrase "SEQ ID NO: 1 and its complement of the same length" as meeting the written description provisions of 35 U.S.C. 112, first paragraph. This was an inadvertent error. SEQ ID NO: 1 is an amino acid sequence, therefore no full length complement exists. To set the record straight, only SEQ ID NO: 1 meets the written description provisions of 35 U.S.C., first paragraph, regarding the sequence portion of this written description issue.

Interview Request

Applicants request a telephonic interview to discuss remaining issues. Applicants are invited to call the Examiner at the phone number listed below to set up an interview time.

Conclusion

Claims 38-43 and 49-59 are not allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and

1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

November 28, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER